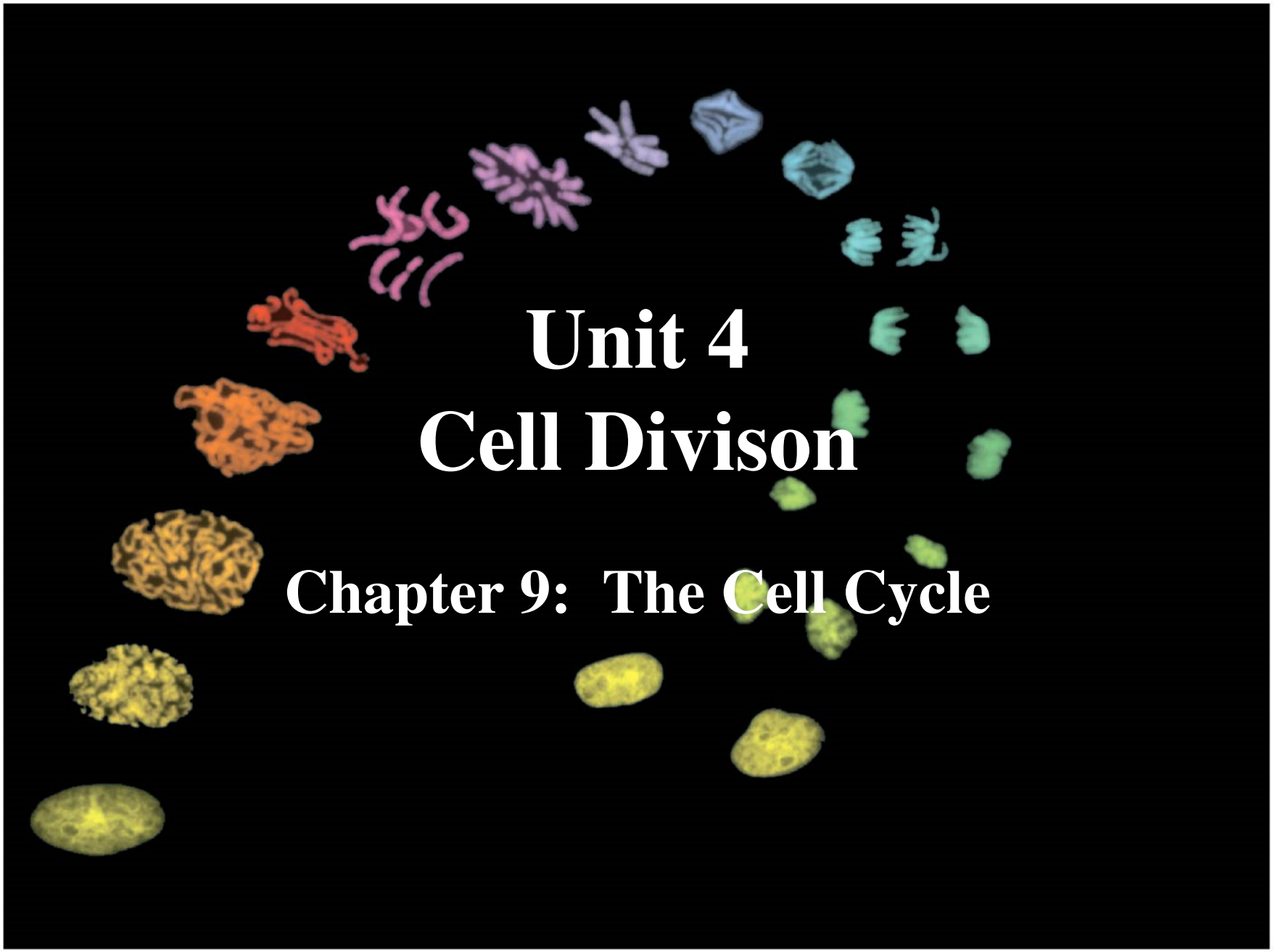


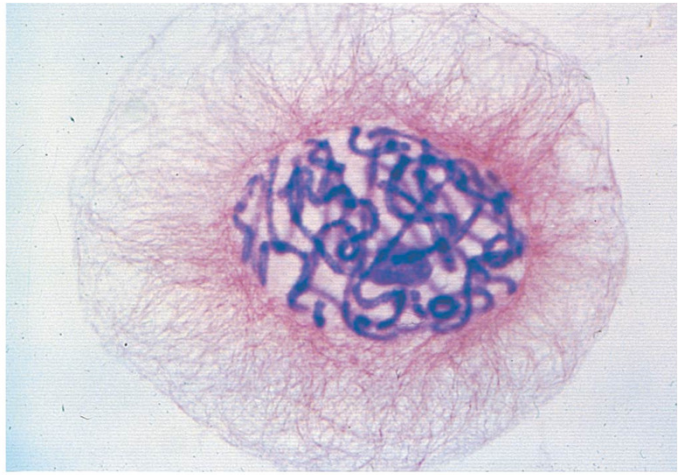
Overview: The Key Roles of Cell Division

- The ability of organisms to produce more of their own kind best distinguishes living things from nonliving matter
- The continuity of life is based on the reproduction of cells, or **cell division**
  - In unicellular organisms, division of one cell reproduces the entire organism
  - Cell division enables multicellular eukaryotes to develop from a single cell and, once fully grown, to renew, repair, or replace cells as needed

- Cell division is an integral part of the **cell cycle**
  - The life of a cell from formation to its own division
- Passing identical genetic material to cellular offspring is a crucial function of cell division!
  - Most cell division results in the distribution of identical genetic material—DNA—to two daughter cells

Concept 9.1: Most cell division results in genetically identical daughter cells

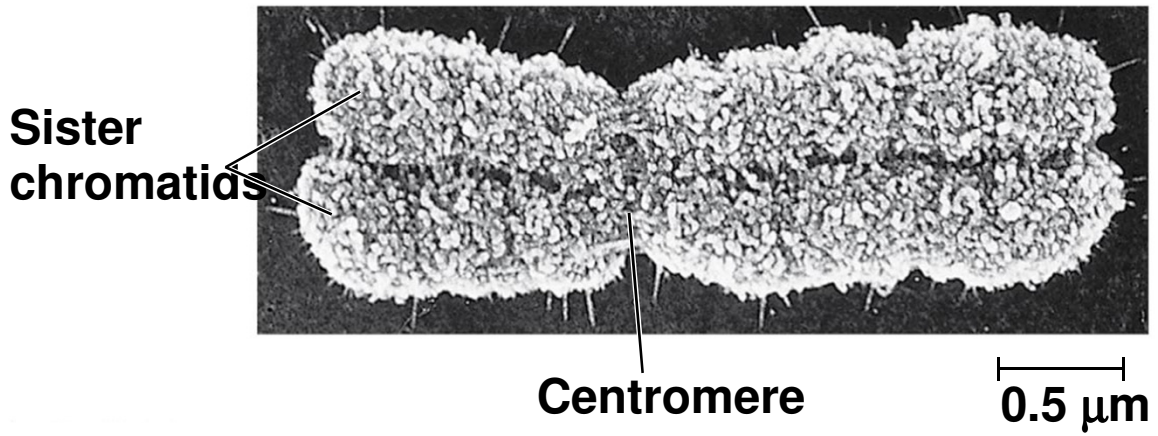
- All the DNA in a cell constitutes the cell's **genome**
  - A genome can consist of a single DNA molecule (common in prokaryotic cells) or a number of DNA molecules (common in eukaryotic cells)
- Before the cell divides, all of this DNA must be copied so each daughter cell ends up with a complete genome
- DNA molecules in a cell are packaged into **chromosomes**



- Eukaryotic chromosomes consist of **chromatin**, a complex of DNA and protein
- Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus
- **Somatic cells** (nonreproductive cells) have two sets of chromosomes
  - Humans: 46 total chromosomes
    - 2 sets of 23 (one set from each parent)
- **Gametes** (reproductive cells: sperm and eggs) have one set of chromosomes
  - Humans: 23 chromosomes

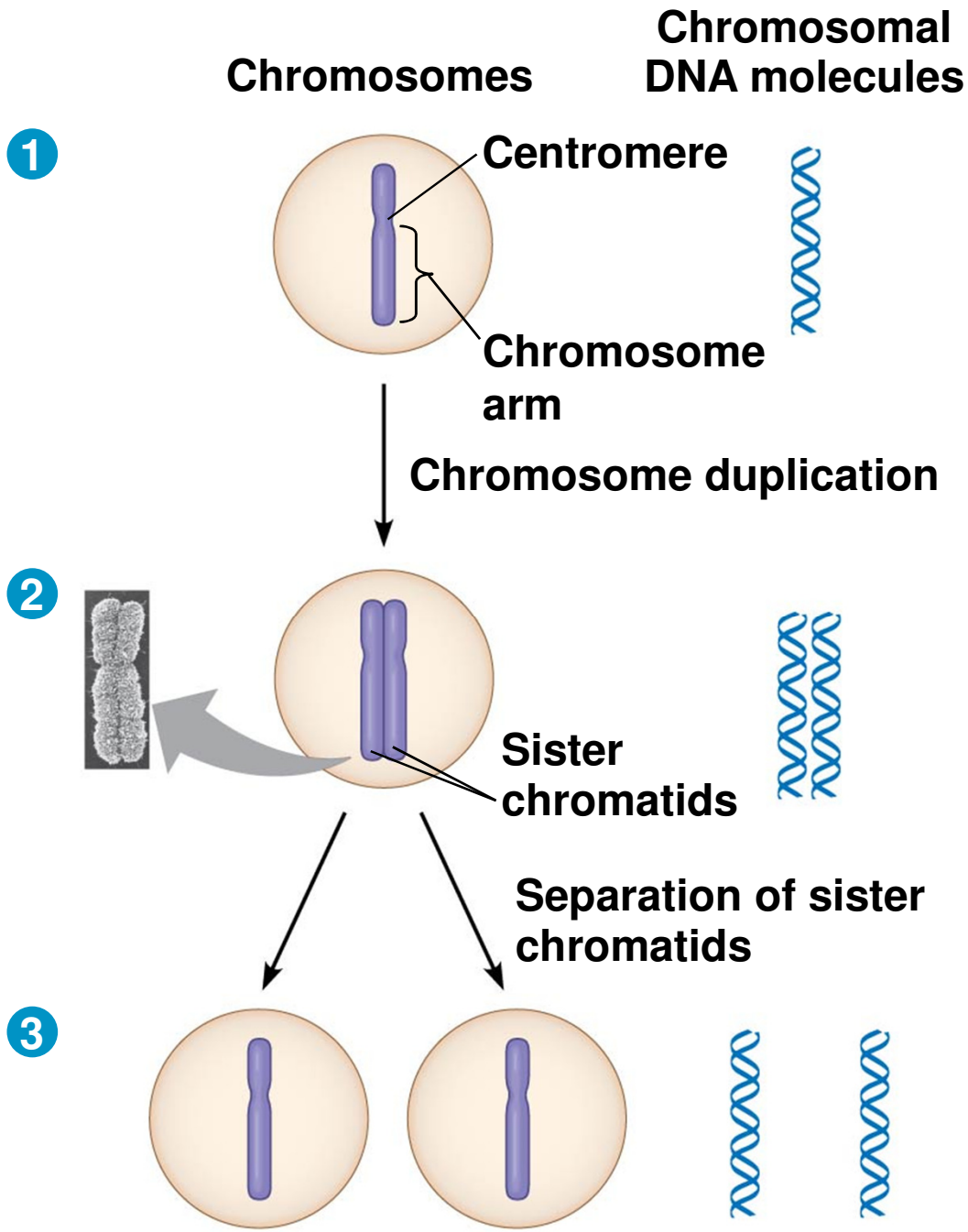
Distribution of Chromosomes During Eukaryotic Cell Division

- In preparation for cell division, DNA is replicated and the chromosomes condense
- Each duplicated chromosome has two **sister chromatids,** joined identical copies of the original chromosome
- The **centromere** is where the two chromatids are most closely attached



- During cell division, the two sister chromatids of each duplicated chromosome separate and move into two nuclei
  - Once separate, the chromatids are called chromosomes
- Thus each new nucleus receives chromosomes identical to that of the parent cell

Figure 9.5-3

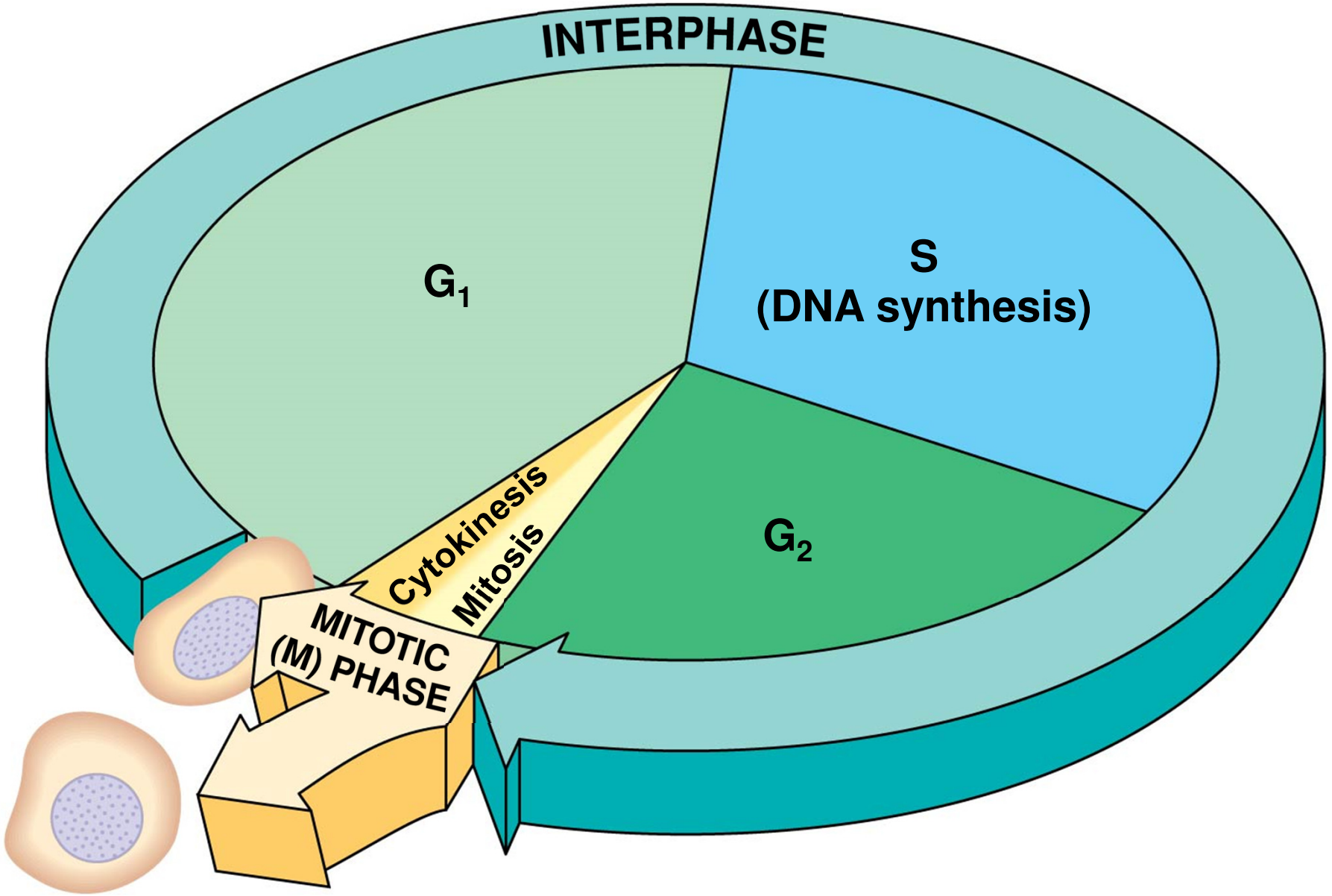

Chromosomes
Chromosomal DNA molecules
1
Centromere
Chromosome arm
Chromosome duplication
2
Sister chromatids
Separation of sister chromatids
3

- Eukaryotic cell division consists of
  - **Mitosis**
    - Division of the genetic material in the nucleus
  - **Cytokinesis**
    - Division of the cytoplasm
- Gametes are produced by a variation of cell division called *meiosis*
  - Meiosis yields nonidentical daughter cells that have only one set of chromosomes, half as many as the parent cell (haploid)
  - *Fertilization* restores diploid number

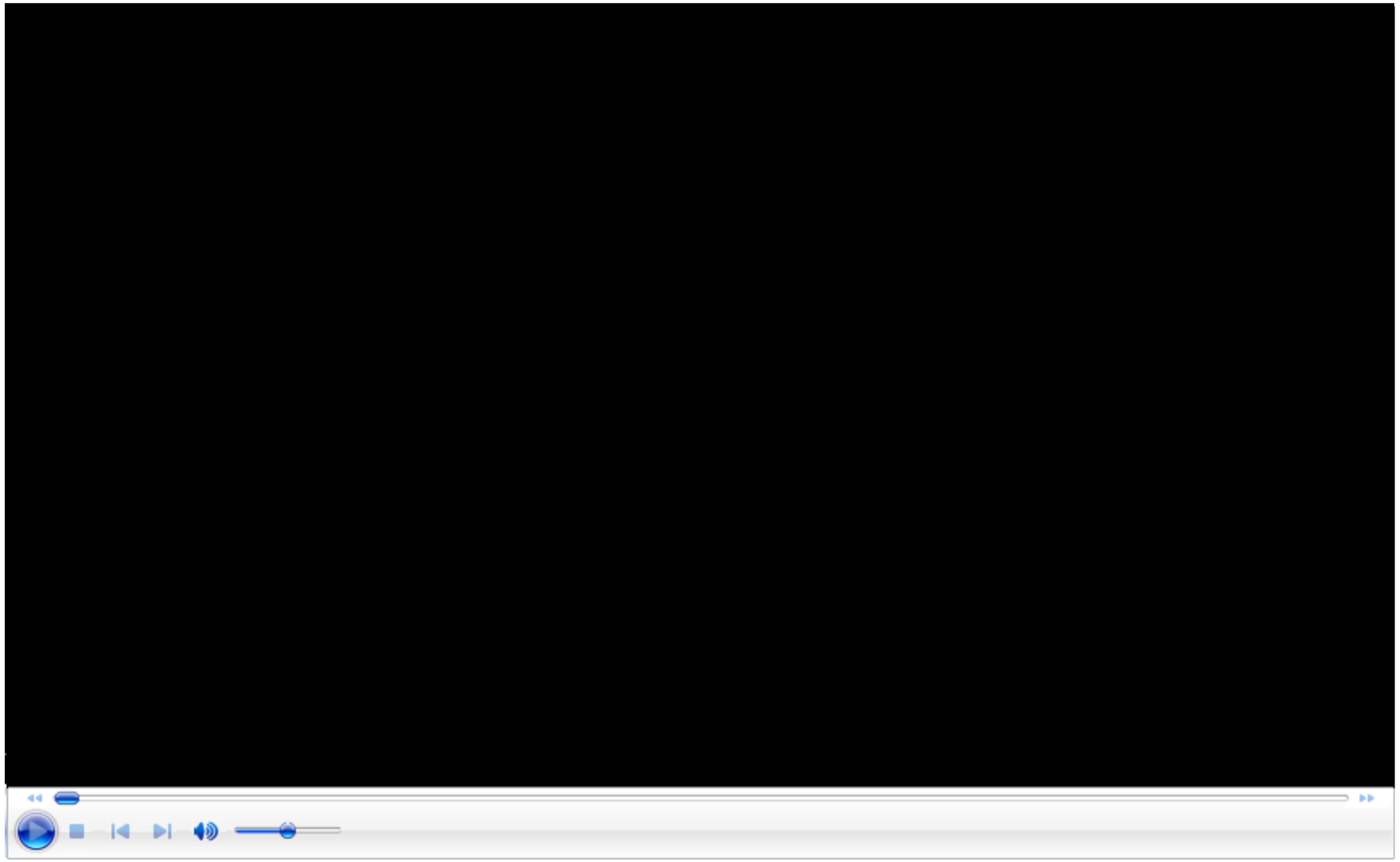
Concept 9.2: The mitotic phase alternates with interphase in the cell cycle

- The cell cycle consists of
  - **Mitotic** (**M**) **phase**, including mitosis and cytokinesis
  - **Interphase**, including cell growth and copying of chromosomes in preparation for cell division
- Interphase (about 90% of the cell cycle) can be divided into subphases
  - **G_1 phase** ("first gap")
  - **S phase** ("synthesis")
  - **G_2 phase** ("second gap")
- Growth during all three phases, but chromosomes are duplicated only during the S phase

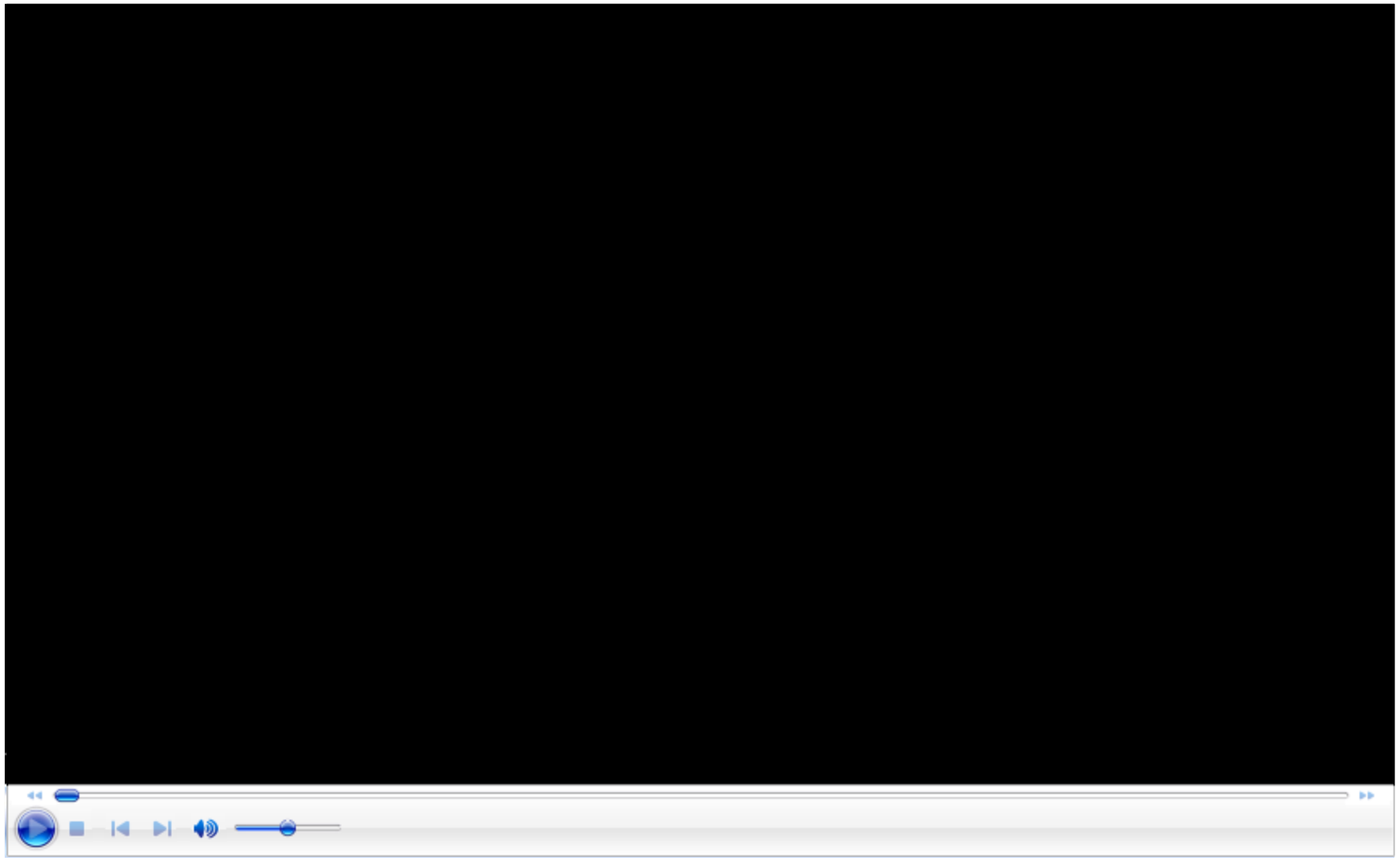
Figure 9.6


INTERPHASE
G1
S
(DNA synthesis)
G2
Cytokinesis
Mitosis
MITOTIC
(M) PHASE

- Mitosis is conventionally divided into five phases
  - **Prophase**
  - **Prometaphase**
  - **Metaphase**
  - **Anaphase**
  - **Telophase**
- Cytokinesis overlaps the latter stages of mitosis



Video: Animal Mitosis



VIDEO: Mitosis

Figure 9.7c

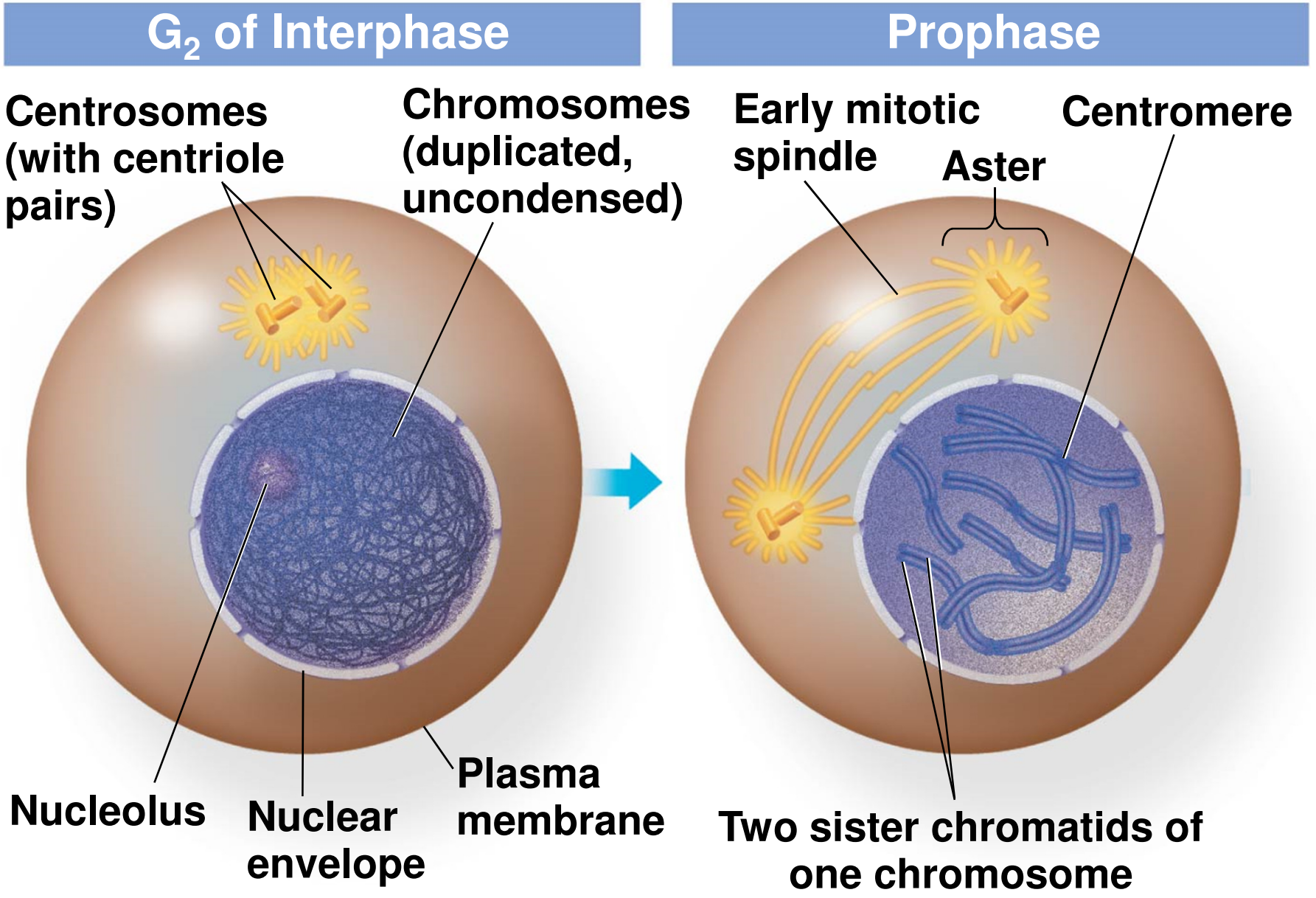

G2 of Interphase
Prophase
Centrosomes (with centriole pairs)
Chromosomes (duplicated, uncondensed)
Early mitotic spindle
Aster
Centromere
Nucleolus
Nuclear envelope
Plasma membrane
Two sister chromatids of one chromosome

Figure 9.7d

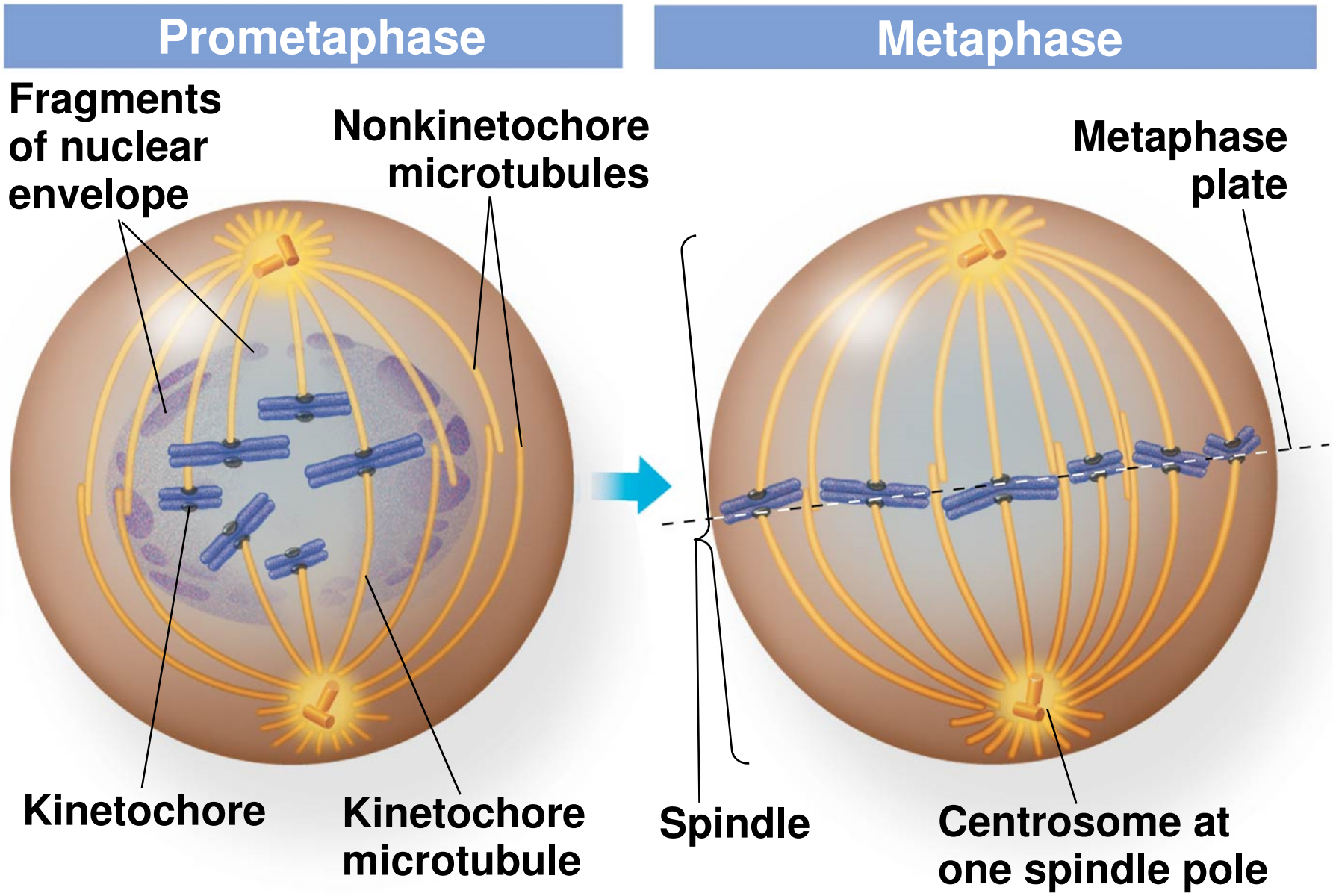
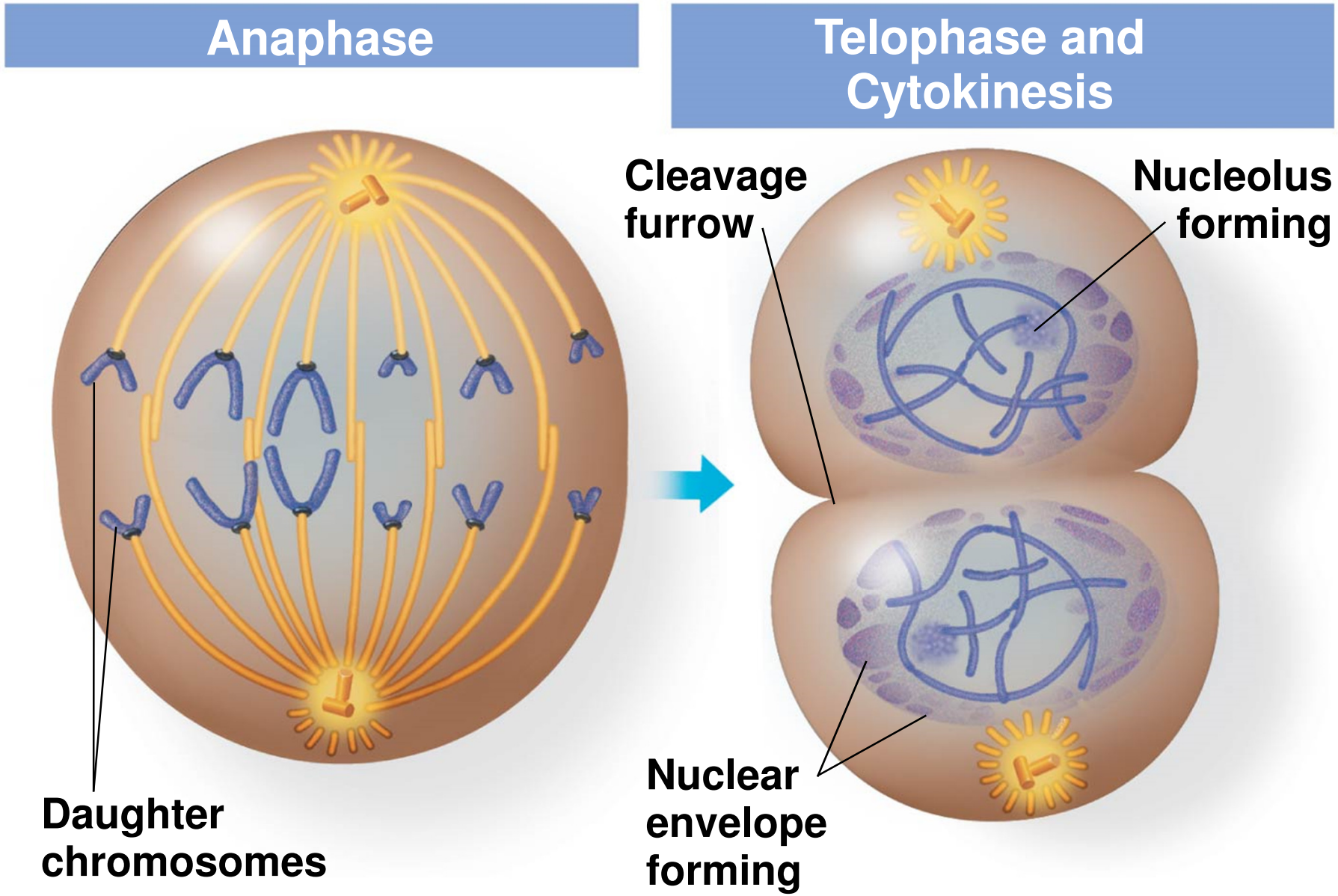

Prometaphase
Metaphase
Fragments of nuclear envelope
Nonkinetochore microtubules
Metaphase plate
Kinetochore
Kinetochore microtubule
Spindle
Centrosome at one spindle pole

Figure 9.7e


Anaphase
Telophase and Cytokinesis
Cleavage furrow
Nucleolus forming
Daughter chromosomes
Nuclear envelope forming

The Mitotic Spindle: *A Closer Look*

- The **mitotic spindle** controls chromosome movement during mitosis
  - Includes the centrosomes, the spindle microtubules, and the asters
- In animal cells, assembly of spindle microtubules begins in the **centrosome**, the microtubule organizing center
  - The centrosome replicates during interphase, forming two centrosomes that migrate to opposite ends of the cell during prophase and prometaphase
- An **aster** (radial array of short microtubules) extends from each centrosome

Prophase

- Chromatin condenses into discrete chromosomes
  - Appear as 2 identical sister chromatids joined at centromere
- Mitotic spindle begins to form
- Centrosomes separate

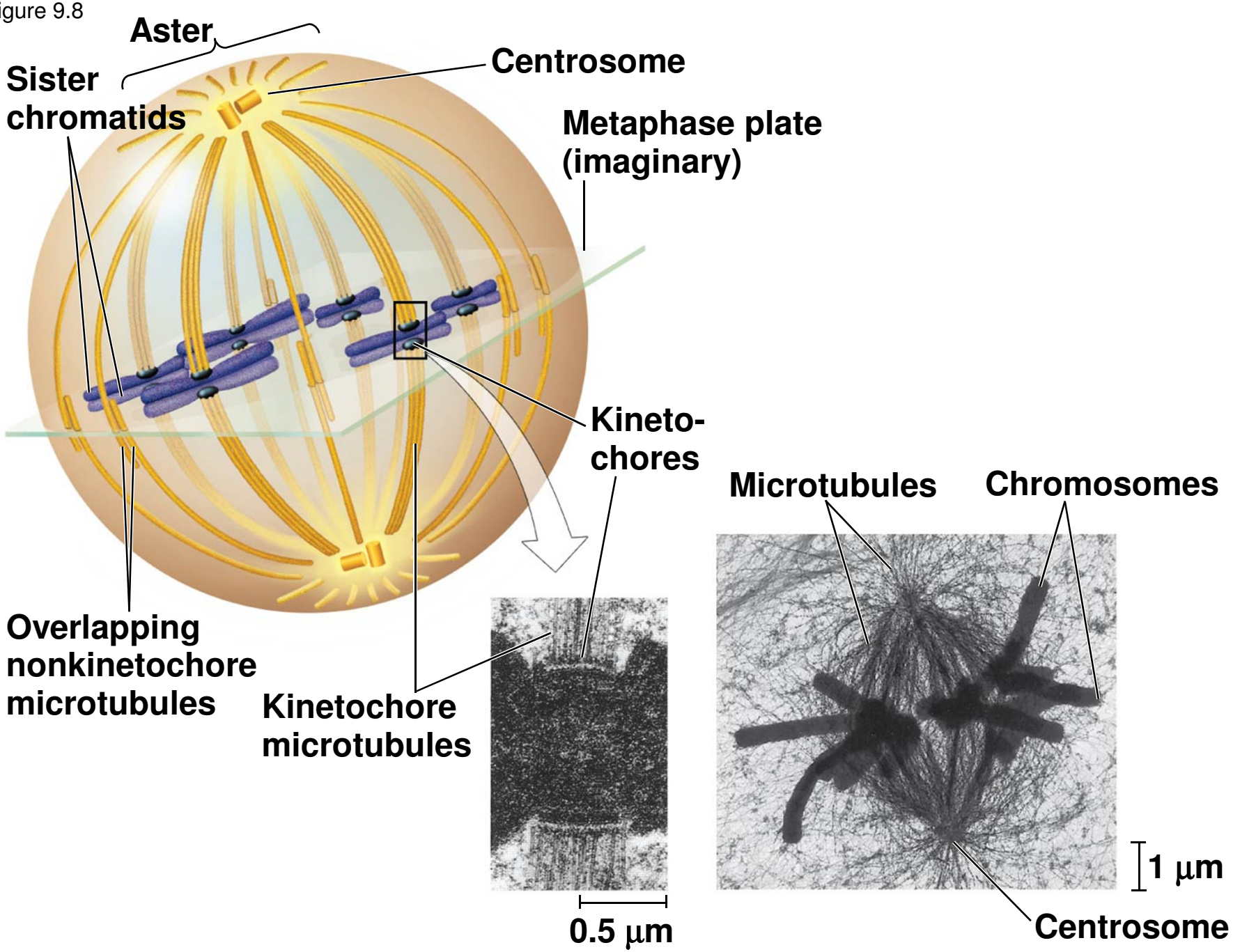
Prometaphase

- Nuclear envelope fragments
- Some spindle microtubules attach to the kinetochores of chromosomes and begin to move the chromosomes
  - **Kinetochores** are protein complexes that assemble on sections of DNA at centromeres

Metaphase

- Chromosomes line up at the **metaphase plate**
  - Imaginary structure at the midway point between the spindle's two poles

Figure 9.8


Aster
Sister chromatids
Centrosome
Metaphase plate (imaginary)
Kineto-chores
Microtubules
Chromosomes
Overlapping nonkinetochore microtubules
Kinetochore microtubules
0.5 μm
1 μm
Centrosome

Anaphase

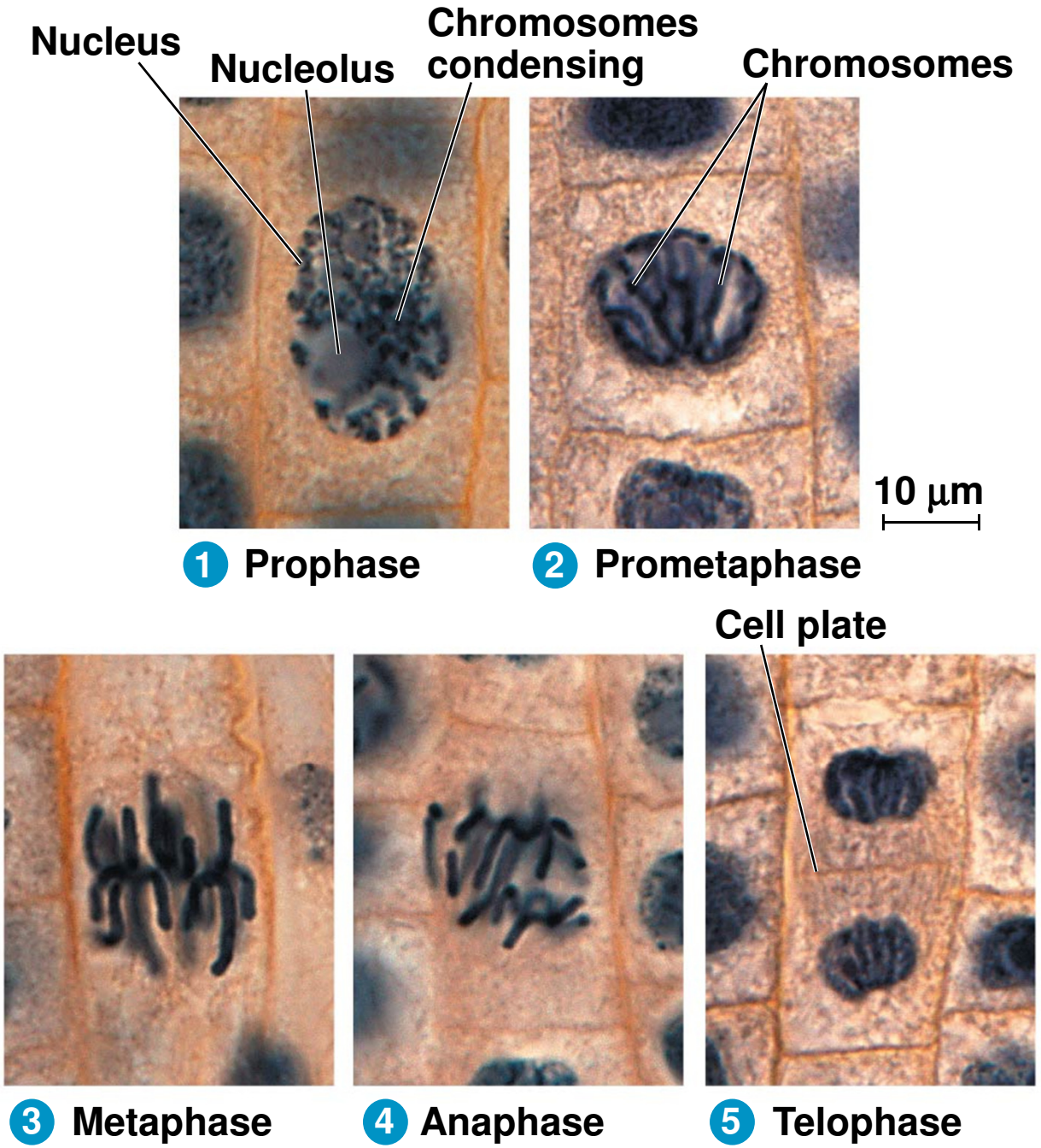
- Sister chromatids separate and move along the kinetochore microtubules toward opposite ends of the cell
  - Chromosomes are also “reeled in” by motor proteins at spindle poles
- Nonkinetochore microtubules from opposite poles overlap and push against each other, elongating the cell
- At the end of anaphase, duplicate groups of chromosomes have arrived at opposite ends of the elongated parent cell

Telophase

- 2 daughter nuclei form in the cell
  - Nuclear envelopes reform

- Cytokinesis begins during anaphase or telophase and the spindle eventually disassembles

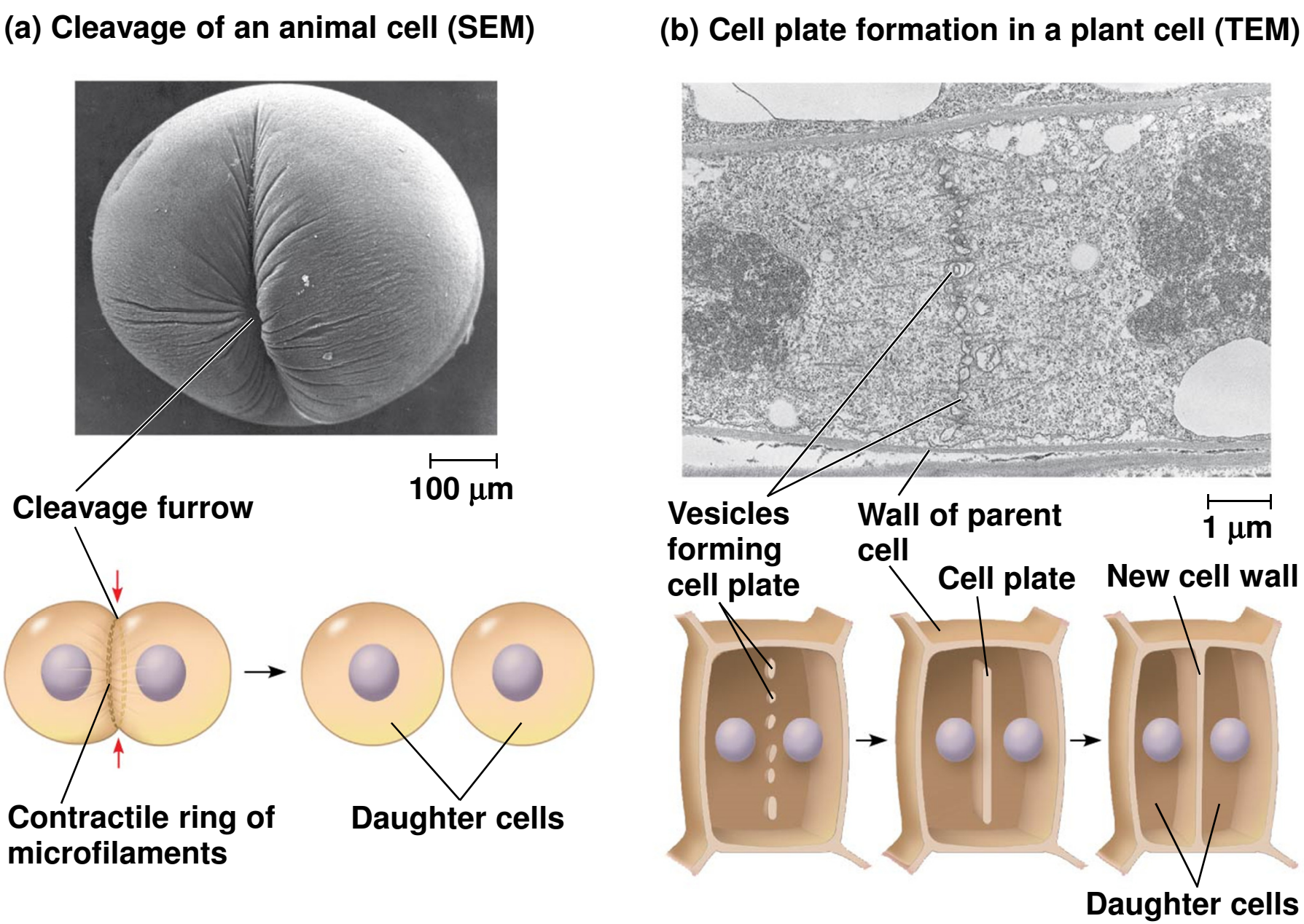
Figure 9.11


Nucleus
Nucleolus
Chromosomes condensing
Chromosomes
10 µm
1 Prophase
2 Prometaphase
Cell plate
3 Metaphase
4 Anaphase
5 Telophase

Cytokinesis: *A Closer Look*

- In animal cells, cytokinesis occurs by a process known as **cleavage**, forming a **cleavage furrow**
  - Shallow groove in cell surface near old metaphase plate
- In plant cells, a **cell plate** forms during cytokinesis
  - Becomes cell wall

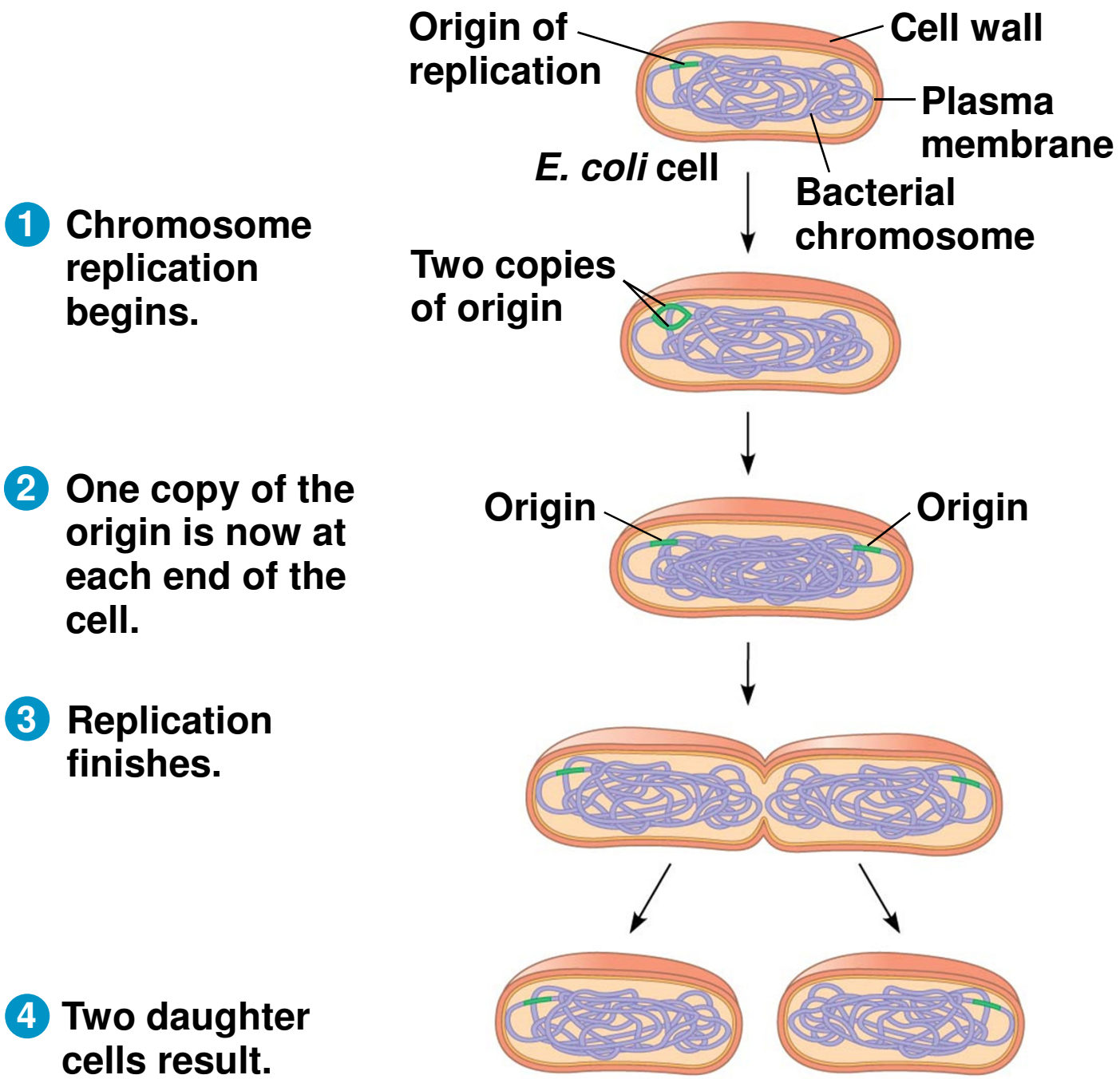
Figure 9.10


(a) Cleavage of an animal cell (SEM)
100 μm
Cleavage furrow
Contractile ring of microfilaments
Daughter cells
(b) Cell plate formation in a plant cell (TEM)
Vesicles forming cell plate
Wall of parent cell
1 μm
Cell plate
New cell wall
Daughter cells

Binary Fission in Bacteria

- Prokaryotes (bacteria and archaea) reproduce by a type of cell division called **binary fission**
  - Asexual reproduction where cell grows and divides into 2 cells
  - Does NOT involve mitosis in prokaryotes
- In *E. coli*, the single chromosome replicates, beginning at the **origin of replication**
- The two daughter chromosomes actively move apart while the cell elongates
- The plasma membrane pinches inward, dividing the cell into two

Figure 9.12-4


Origin of replication
Cell wall
Plasma membrane
E. coli cell
Bacterial chromosome
Two copies of origin
Origin
Origin
1 Chromosome replication begins.
2 One copy of the origin is now at each end of the cell.
3 Replication finishes.
4 Two daughter cells result.

The Evolution of Mitosis

- Since prokaryotes evolved before eukaryotes, mitosis probably evolved from binary fission
- Certain protists (dinoflagellates, diatoms, and some yeasts) exhibit types of cell division that seem intermediate between binary fission and mitosis

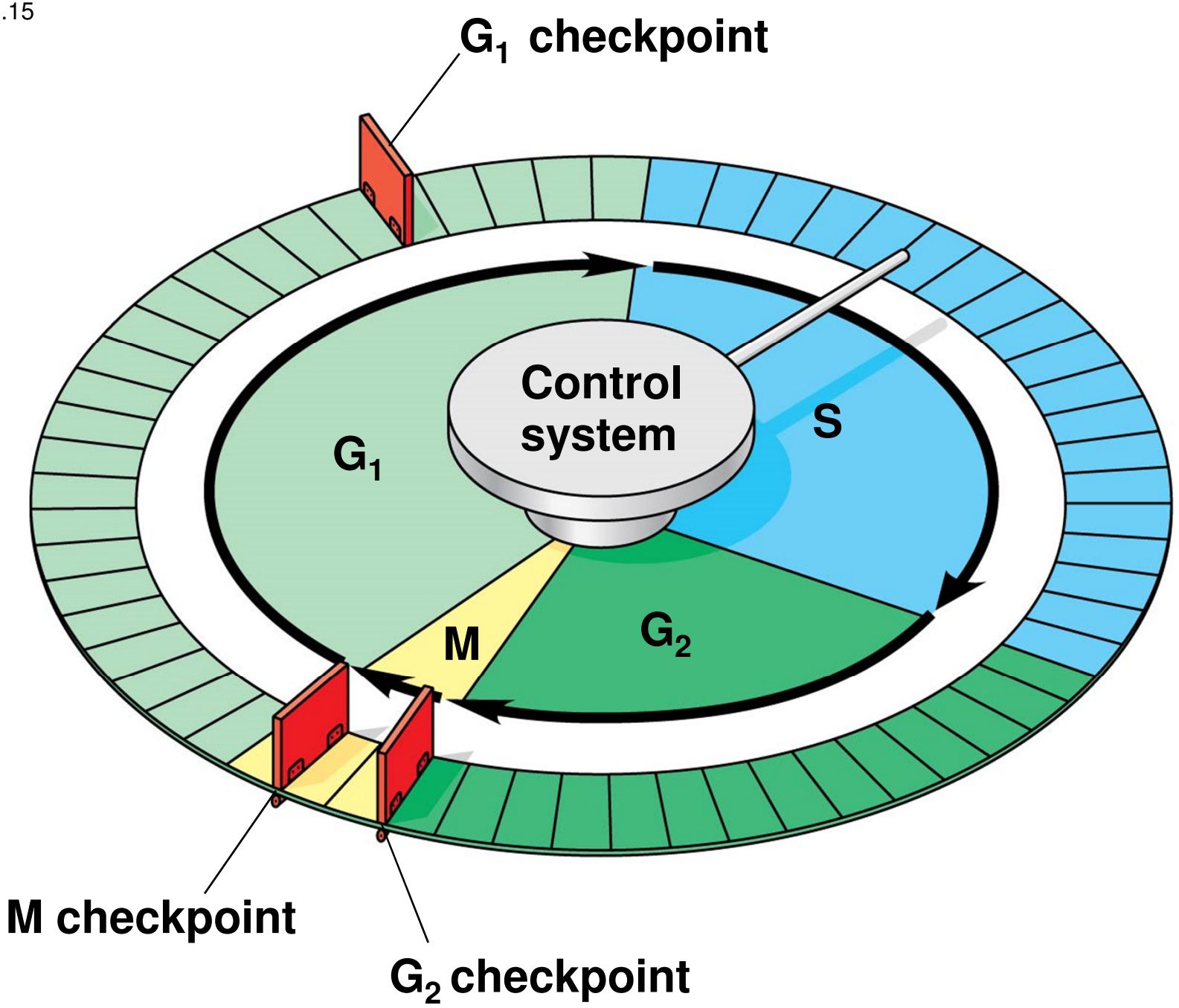
Concept 9.3: The eukaryotic cell cycle is regulated by a molecular control system

- The frequency of cell division varies with the type of cell
  - Human skin cells divide frequently
  - Fully formed nerve and muscle cells do not divide at all when mature
- These differences result from regulation at the molecular level
- Cancer cells manage to escape the usual controls on the cell cycle

Checkpoints of the Cell Cycle Control System

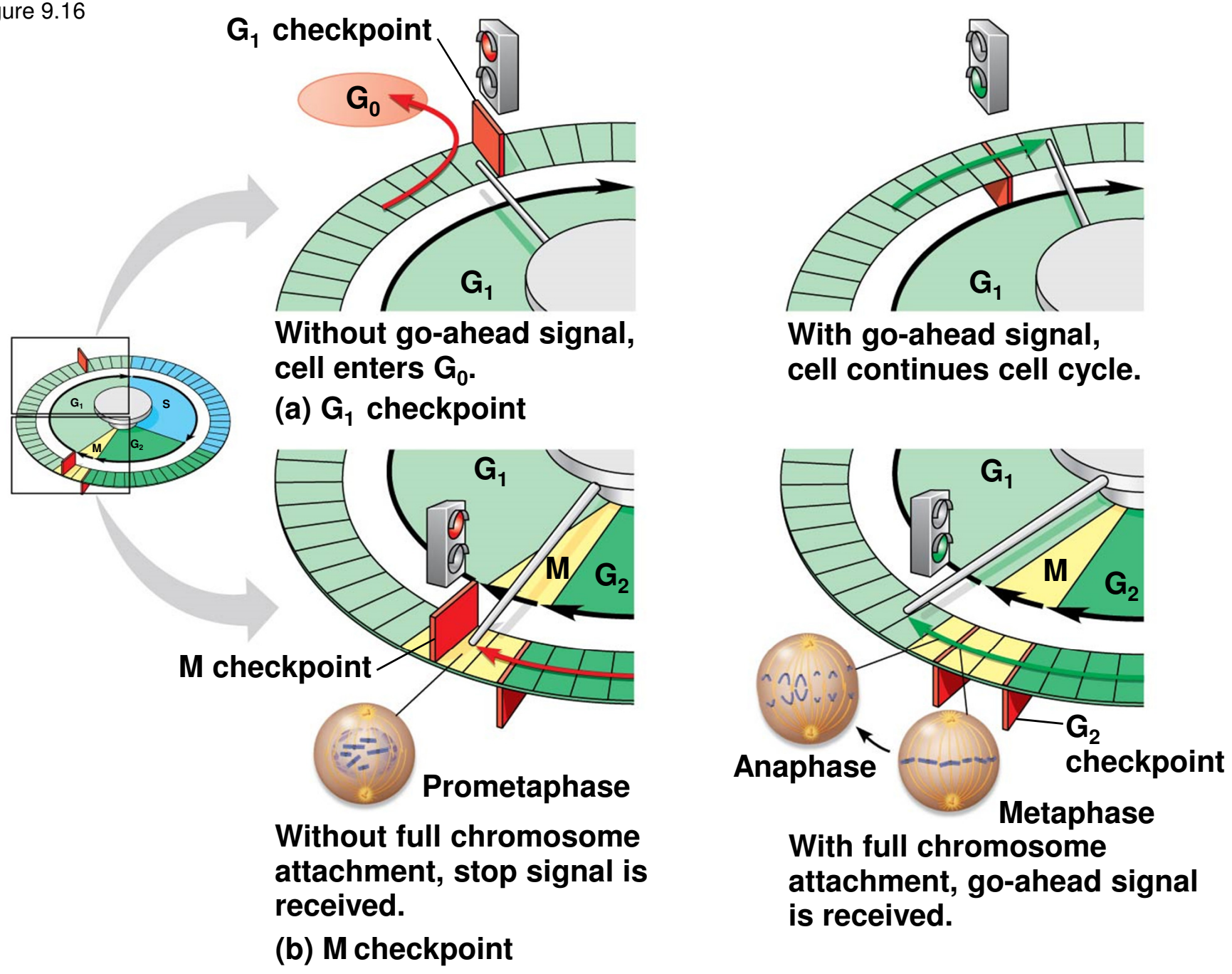
- The cell cycle is driven by specific signaling molecules present in the cytoplasm
- The sequential events of the cell cycle are directed by a distinct **cell cycle control system**, which is similar to a timing device of a washing machine
  - The cell cycle control system is regulated by both internal and external controls
- The clock has specific **checkpoints** where the cell cycle stops until a go-ahead signal is received

Figure 9.15


G_1 checkpoint
Control system
G_1
S
M
G_2
M checkpoint
G_2 checkpoint

- For many cells, the G_1 checkpoint seems to be the most important
  - If a cell receives a go-ahead signal at the G_1 checkpoint, it will usually complete the S, G_2, and M phases and divide
  - If the cell does not receive the go-ahead signal, it will exit the cycle, switching into a nondividing state called the **G_0 phase**
- The cell cycle is regulated by a set of regulatory proteins and protein complexes including kinases and proteins called cyclins

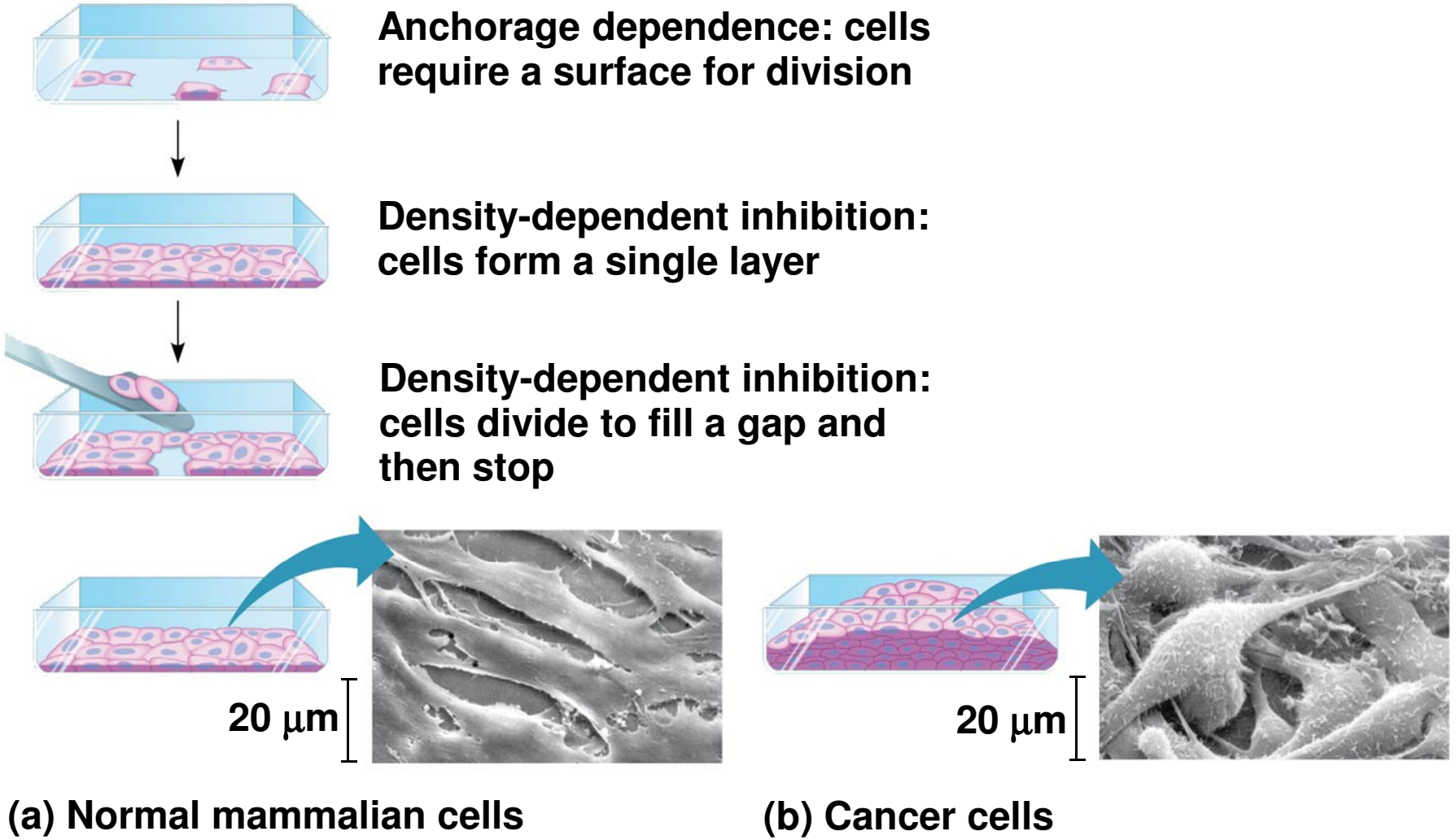
Figure 9.16


G1 checkpoint
G0
G1
Without go-ahead signal, cell enters G0.
(a) G1 checkpoint
G1
With go-ahead signal, cell continues cell cycle.
G1
S
G2
M
G1
M
G2
M checkpoint
Prometaphase
Without full chromosome attachment, stop signal is received.
(b) M checkpoint
G1
M
G2
Anaphase
G2 checkpoint
Metaphase
With full chromosome attachment, go-ahead signal is received.

- An example of an internal signal occurs at the M phase checkpoint
  - In this case, anaphase does not begin if any kinetochores remain unattached to spindle microtubules
- Attachment of all of the kinetochores activates a regulatory complex, which then activates the enzyme separase
  - Separase allows sister chromatids to separate, triggering the onset of anaphase
- Ensures that daughter cells do not end up with missing or extra chromosomes

- Some external signals are **growth factors**, proteins released by certain cells that stimulate other cells to divide
- Another example of external signals is **density-dependent inhibition**
  - Crowded cells stop dividing
- Most animal cells also exhibit **anchorage dependence**
  - Cells must be attached to a substratum in order to divide
- Cancer cells exhibit neither density-dependent inhibition nor anchorage dependence

Figure 9.18

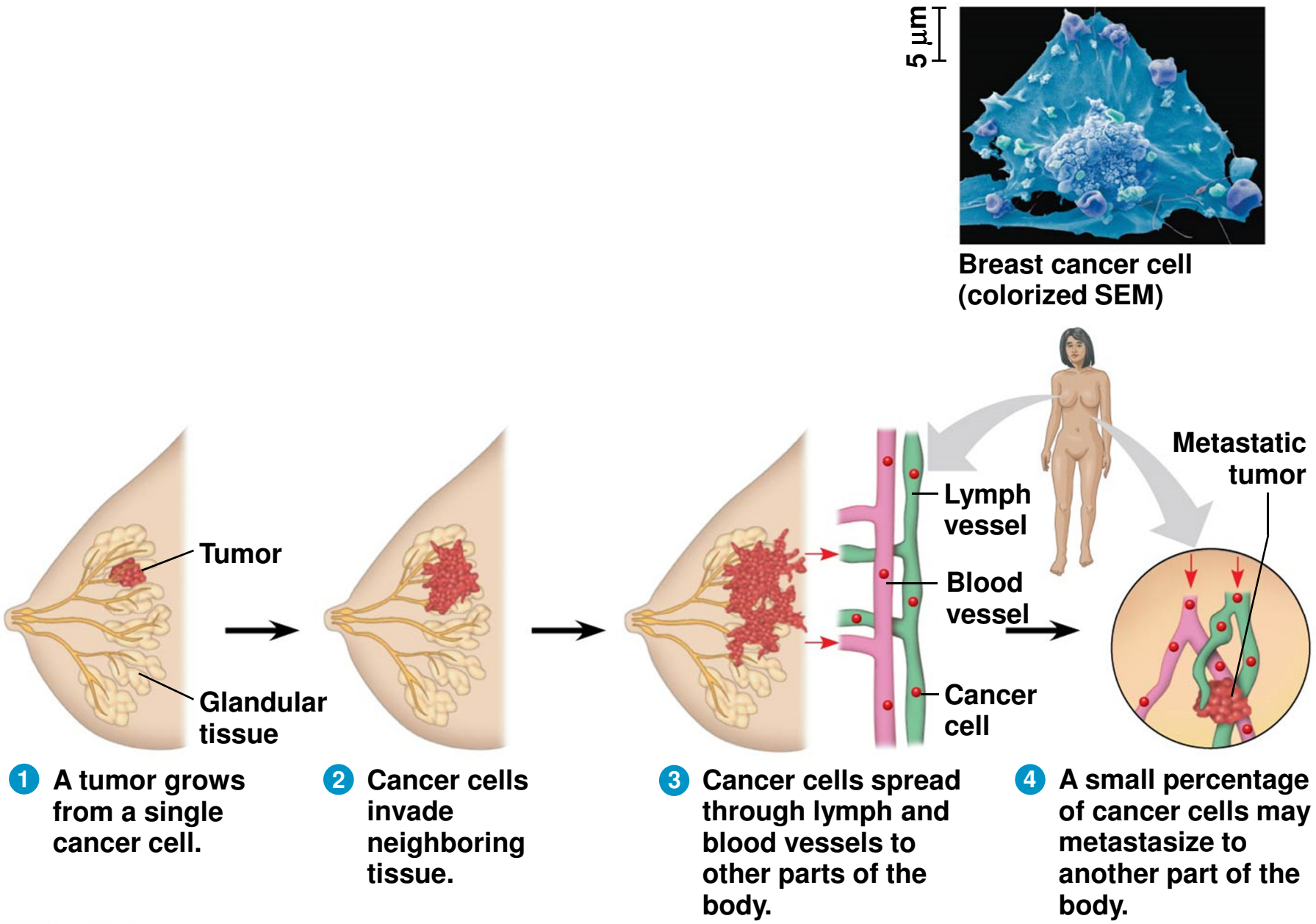

Anchorage dependence: cells require a surface for division
Density-dependent inhibition: cells form a single layer
Density-dependent inhibition: cells divide to fill a gap and then stop
20 μm
20 μm
(a) Normal mammalian cells
(b) Cancer cells

Loss of Cell Cycle Controls in Cancer Cells

- Cancer cells do not respond to signals that normally regulate the cell cycle
- Cancer cells may not need growth factors to grow and divide
  - They may make their own growth factor
  - They may convey a growth factor's signal without the presence of the growth factor
  - They may have an abnormal cell cycle control system

- A normal cell is converted to a cancerous cell by a process called **transformation**
- Cancer cells that are not eliminated by the immune system form tumors, masses of abnormal cells within otherwise normal tissue
  - If abnormal cells remain only at the original site, the lump is called a **benign tumor**
  - **Malignant tumors** invade surrounding tissues and can **metastasize**, exporting cancer cells to other parts of the body, where they may form additional tumors

Figure 9.19


5 µm
Breast cancer cell
(colorized SEM)
Tumor
Glandular tissue
Lymph vessel
Blood vessel
Cancer cell
Metastatic tumor
1 A tumor grows from a single cancer cell.
2 Cancer cells invade neighboring tissue.
3 Cancer cells spread through lymph and blood vessels to other parts of the body.
4 A small percentage of cancer cells may metastasize to another part of the body.

- Recent advances in understanding the cell cycle and cell cycle signaling have led to advances in cancer treatment
- Medical treatments for cancer are becoming more “personalized” to an individual patient’s tumor
- One of the big lessons in cancer research is how complex cancer is